PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of: Attorney Docket No.: 48577.2.1

Filtvedt, et al.

Application No.: 10/749,150 Examiner: Huong Q. Pham

Filed: December 30, 2003 Group Art Unit: 3743

For: DEVICE FOR APPLYING A PULSATING PRESSURE TO A LOCAL REGION OF THE BODY AND THE APPLICATIONS THEREOF

RULE 1.132 AFFIDAVIT OF ERLING BEKKESTAD REIN

Erling Bekkestad Rein, being first duly sworn, deposes and says:

A. Background

I am Erling Bekkestad Rein. I am a licensed medical doctor in Norway. To earn my licensure, I completed six years of medical school at the University of Oslo and two years of hospital internship. While in medical school, I received a scholarship from the Norwegian Army to conduct research on cardiovascular physiology in the Department of Physiology at the Institute of Basic Medical Sciences. Before medical school, I was a medical officer in the Norwegian Army, having graduated from the Norwegian Military Academy.

Currently, I am pursuing my Ph.D. at the University of Oslo. My thesis is on blood circulation and mechanisms in temperature regulation. The main method in my work is ultrasound Doppler. Our research group uses modern, non-invasive methods combined with advanced data processing techniques in our research. We have focused particularly on the rapid responses of the human cardiovascular system to different stimuli and the control mechanisms underlying these responses. At present, the group is working on the skin circulation and temperature regulation, short-term control of the central circulation and blood pressure, and muscle blood flow.

B. Purpose

I am submitting this Affidavit to explain the significance of applying pulses of negative pressure to a local region of a body at the claimed intervals.

C. The Claimed Intervals

The pending claims recite different combinations of intervals. In many claims, negative pressure is generated for between 1 and 20 seconds and released for between 2 and 15 seconds. Some claims require a smaller range of time for pressure generation, such as between 5 and 15 seconds or for 10 seconds. Likewise, some claims require a smaller range of time for pressure release, such as between 5 and 10 seconds or for 7 seconds.

D. Comparison of the Claimed Intervals to Those of the Cited References

Applying pulses of negative pressure to a local region of a body at the claimed intervals is novel over the cited references. Pulses of negative pressure cause blood vessels to dilate, thereby providing for increased blood velocity through those blood vessels. Pulses at the claimed intervals cause optimum blood velocity increases over an extended period of time. The following table highlights the relevant pulse intervals from the cited references, with the first column listing the cited reference and the second column providing the negative pressure pulse interval disclosed in that reference:

Cited Reference	Disclosed Negative Pressure Pulse Interval
MacLeod (3,292,613)	Pressure generation and pressure release occur for each heartbeat (i.e., approximately every second) (column 5, lines 9-20)
MacLeod (3,094,983)	Pressure generation and pressure release occur for each heartbeat (i.e., approximately every second) (column 1, lines 31-33)
Norton et al (3,878,839)	Pressure generation and pressure release occur for each heartbeat (i.e., approximately every second) (column 9, line 63 through column 10, line 13)
Grahn (5,683,438)	Pressure generation and pressure release occur

	for each heartbeat (i.e., approximately every second) (column 5, lines 33-34)
McGrath (3,896,794)	Not applicable because pressure pulses are positive (column 4, line 63 through column 5, line 2)
Christoffel (4,186,732)	Not applicable because pressure pulses are positive (column 1, lines 54-68)

Thus, as is shown, the claimed negative pressure pulse intervals referenced in Section C are not disclosed or taught in any of the cited references.

E. Impact of the Claimed Negative Pressure Pulse Intervals on Blood Velocity

Applying pulses of negative pressure to a local region of a body at the claimed intervals produces remarkable increases in blood velocity within that region. This is shown by an experiment conducted by my co-inventors and me in accordance with the invention disclosed in the present application. The following sections explain the experiment, provide the resulting data, and analyze that data. The results show that applying pulses of negative pressure at the claimed intervals has a remarkable impact on blood velocity, while doing so at other intervals does not.

1. The Experiment

Seven patients each placed his/her right arm inside a pressure tube as is shown in Figure 1.

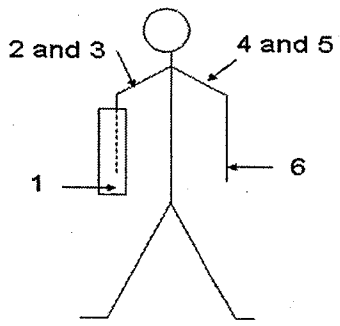


Figure 1

Blood velocity, blood pressure, and tube pressure measurements were recorded with a pulsed ultrasound Doppler machine. Blood velocity measurements were taken in arteries located at 2 and 3 for the right arm ("tube-arm") and at 4 and 5 for the left arm ("control-arm"). These arteries supply blood to the skin of the lower arms. In addition, blood pressure measurements were taken at location 6, and tube pressure measurements were taken at location 1.

2. The Resulting Data

Figure 2, which includes five plots, shows recordings for one representative patient:

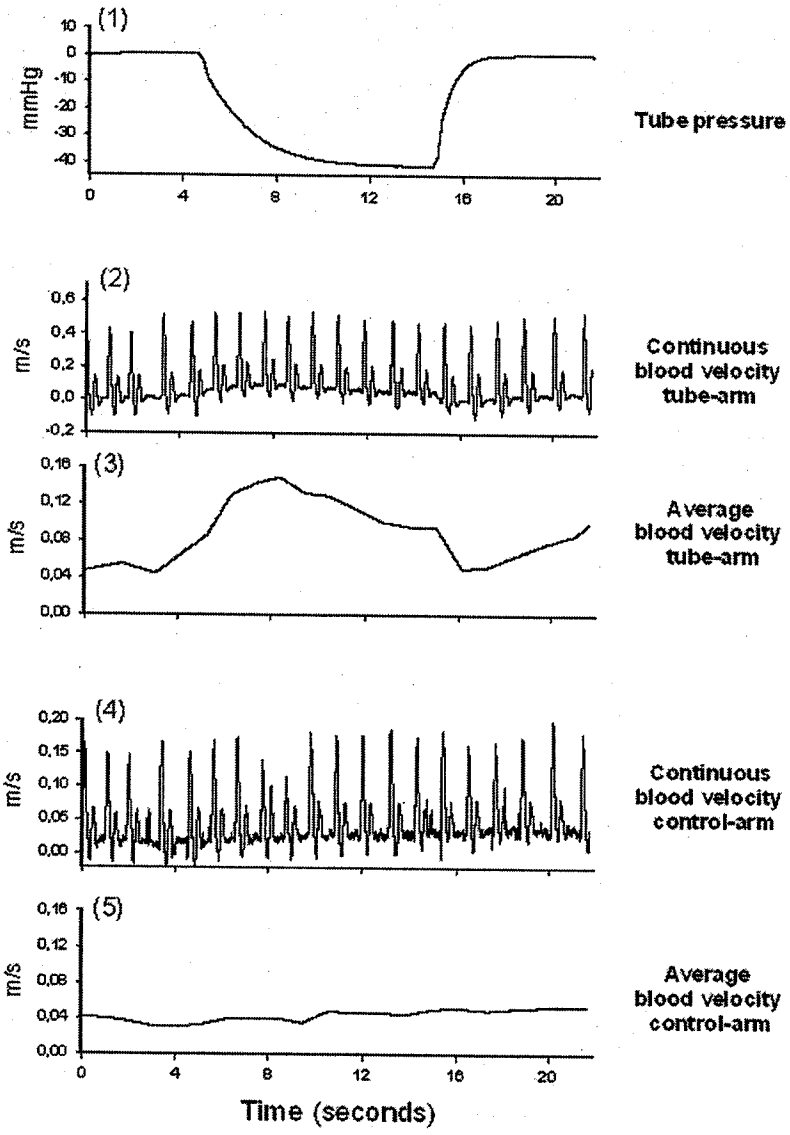


Figure 2

- Plot 1 shows a recording of one negative pressure pulse applied to the tube. The negative pressure pulse falls within the claimed intervals, as negative pressure is generated for 10 seconds (seconds 5-14) and released for 7 seconds (seconds 15-21).
- Plot 2 shows the blood velocity of the tube-arm taken on a continuous basis.
- Plot 3 shows the average blood velocity of the tube-arm calculated every second.
- Plot 4 shows the blood velocity of the control-arm taken on a continuous basis.
- Plot 5 shows the average blood velocity of the control-arm calculated every second.

Figure 3A shows average recordings for all seven of the patients when subjected to three types of negative pressure: (1) no negative pressure, (2) constant negative pressure, and (3) pulses of negative pressure falling within the scope of the present application's pending claims:

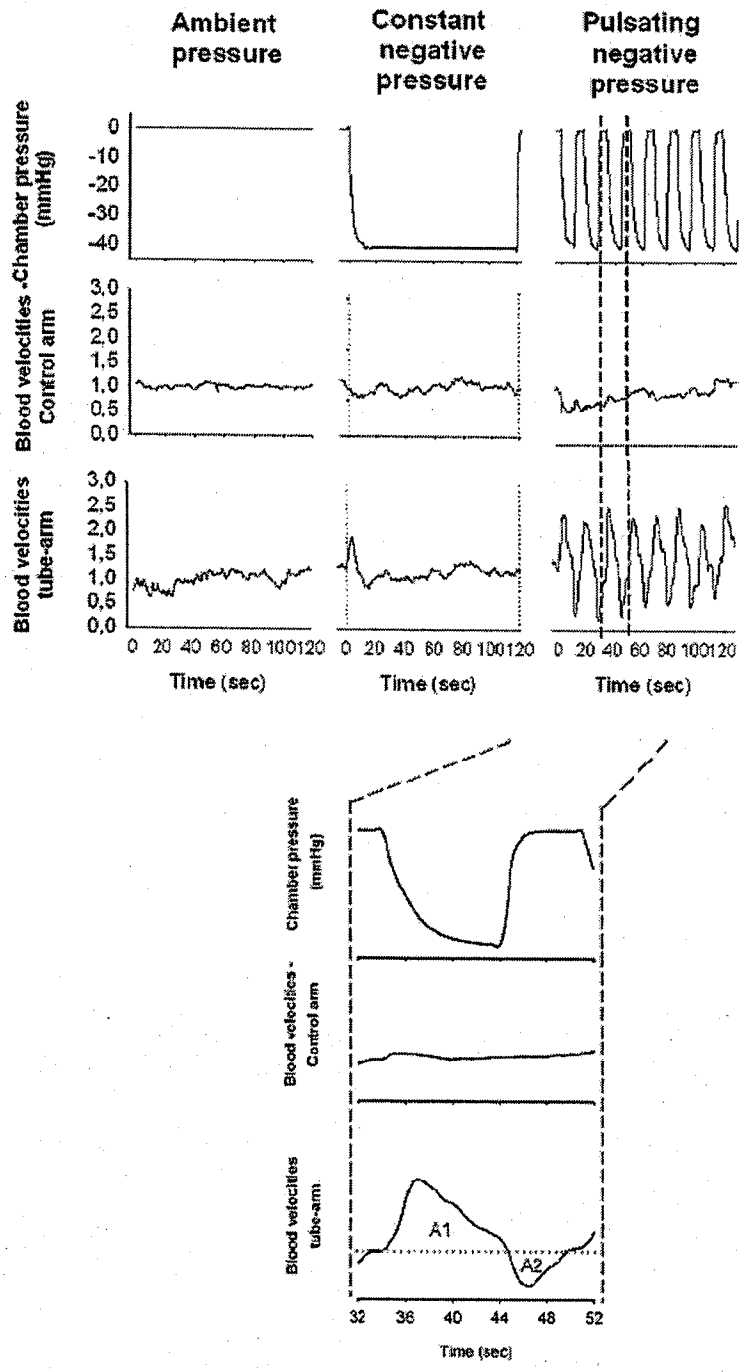


Figure 3A

For each type of pressure, measurements were taken of the tube pressure, the control-arm average blood velocity, and the tube-arm average blood velocity. The blood velocities are shown in comparison to a baseline blood velocity designated 1.0. As can be seen, the lower portion of Figure 3A magnifies a period of time when the patients were subjected to a full pulse of negative pressure falling within the scope of the present application's pending claims.

Figure 3B provides a magnified view of two important average recordings of Figure 3A:

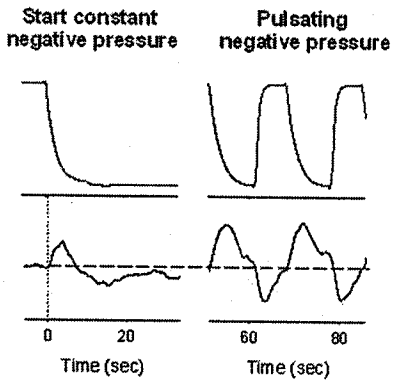
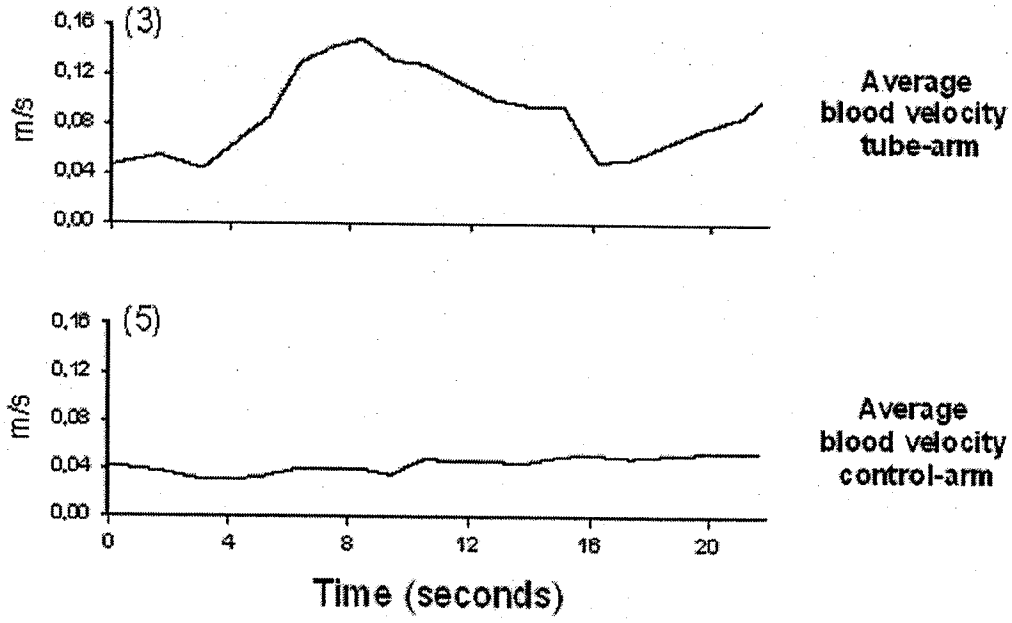


Figure 3B

The left column shows tube pressure and tube-arm average blood velocity when exposed to constant negative pressure. The right column shows those same measurements when exposed to pulses of negative pressure falling within the scope of the present application's pending claims.

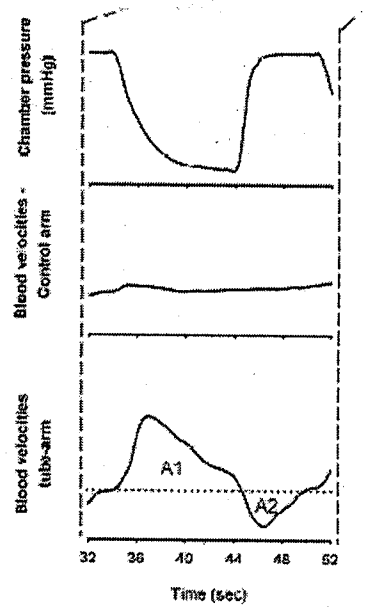
3. Analysis

The results of our experiment show that when applying pulses of negative pressure, doing so at the claimed intervals has a remarkable impact on blood velocity while doing so at other intervals has no appreciable impact. Comparing plot 3 with plot 5 of Figure 2 demonstrates the remarkable impact that the present invention has on blood velocities.



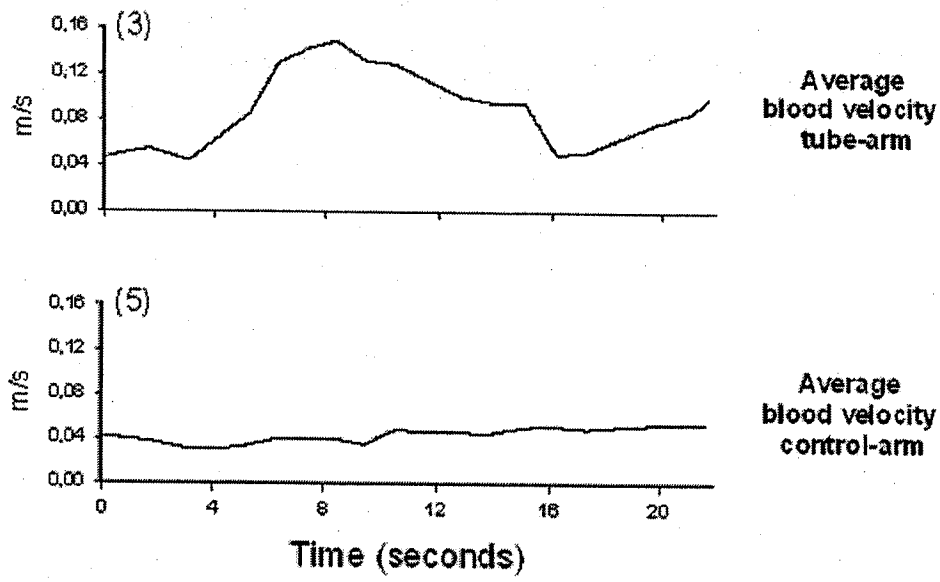
As can be seen, while the control-arm's average blood velocity hovers around 0.04 m/s, the tube-arm's average velocity increases to nearly 0.16 m/s—a nearly 400% increase! Moreover, the tube-arm's average blood velocity remains greater than that of the control-arm for the entire duration of pressure generation, as opposed to spiking up to a maximum level and quickly returning to normal.

The longer-term benefits are confirmed by viewing the lower portion of Figure 3A:



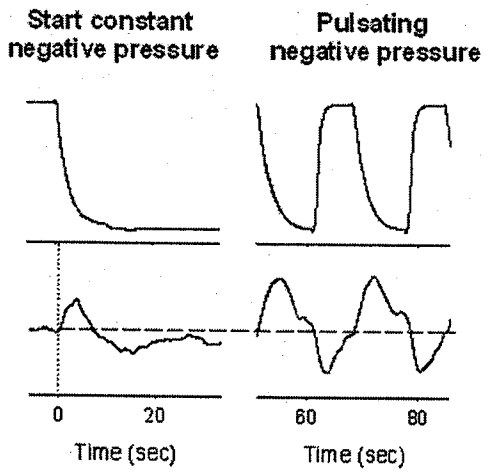
As can be seen, average blood velocity in the tube-arm is increased during pressure generation (A1) and decreased during pressure release (A2). But, as can also be seen, A1 is substantially greater than A2, meaning that the net impact of one pressure pulse is a substantial increase in average blood velocity. In fact, we have estimated the net increase in blood velocity to be greater than 50%.

In contrast, plot 3 of Figure 2 illustrates how applying a negative pressure for too short a duration misses the benefits associated with the present invention.



Under the conditions of our experiment, the average blood velocity in the tube-arm increased sharply during the first 4 seconds of negative pressure and remained higher than that of the control-arm for the next 6 seconds. During this period, the heart contracted 4-6 times. These numbers will vary under other conditions disclosed in the present application. Removing the negative pressure too soon does not allow blood velocity to build up to the point where benefits are realized. The blood vessels do not have time to adjust to the change in pressure. Accordingly, negative pressure must be applied for at least a full second in order to reap the benefits associated with the present invention.

Likewise, Figure 3B illustrates how applying negative pressure for too long a duration misses the benefits associated with the present invention:



Under the conditions of our experiment, after negative pressure has been applied for roughly 10 seconds, the average blood velocity falls below the baseline, indicating decreased blood velocity. The average blood velocity then remains lower than the baseline until the pressure is released. These numbers will vary under other conditions disclosed in the present application. The reason for this decrease is that continuous negative pressure triggers a reflex that causes the arterioles to constrict, thereby significantly decreasing blood velocity. Accordingly, negative pressure should not be applied for more than 20 seconds in order to reap the benefits associated with the present invention.

F. Article Published in the British Journal of Anaesthesia

Attached as Exhibit 1 to this Affidavit is a true and correct copy of an article published in the British Journal of Anaesthesia on January 26, 2007. The article is titled "Hypothermia During Laparotomy Can Be Prevented by Locally Applied Warm Water and Pulsating Negative Pressure." I am the first author listed in the article. This article discusses further experiments that confirm that applying negative pressure pulses to a local region of a body produces remarkable increases in blood velocity in that region.

G. Contract with the U.S. Navy

In November of 2006, my company, Thermonor AS, entered into a contract with the U.S. Navy under which we will deliver five commercial embodiments of the present invention to the

U.S. Navy for evaluation. In exchange, we will receive $500,000. The United States Congress appropriated the funding in the 2007 Defense Appropriations Bill.

H. Conclusion

For the reasons set forth above, applying pulses of pressure to a local region of a body at the claimed intervals distinguishes the pending claims over the cited references and produces remarkable increases in blood velocity in the relevant local region.

Erling Bekkestad Rein

Erling Bekkestad Rein

STATEMENT BY WITNESS FOR ERLING BEKKESTAD REIN

I, METTE HAMMERSLAND MJELDE whose full post office address is HAGA, 5650 TYSSE, NORWAY was personally present and did see Erling Bekkestad Rein, who is known to me, execute the above affidavit.

Mette H. Mjelde

(Signature of Witness)

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EXHIBIT 1

E . Advance Access published January . , 2007

British Journal of Anaesthesia Page 1 of 6
doi:10.1093/bja/ael369

BJA

Hypothermia during laparotomy can be prevented by locally applied warm water and pulsating negative pressure

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Background. Conflicting results have been obtained when using heat and constant negative pressure applied to the arm to induce re-warming in patients with mild hypothermia due to surgery. We hypothesized that pulsating negative pressure would increase skin blood flow and thus heat transfer. The purpose of this study was to compare a new method of applying heat and pulsating negative pressure to the skin with conventional forced-air warming for preventing perioperative hypothermia.

Methods. Twenty patients undergoing prolonged laparotomy for gastric surgery were randomized into two groups. One group (SM) received hospital standard method: forced-air warming, 43°C (Bair Hugger®) on the thoracic and upper arm surface. The other group (NM) received the new method: warm water and pulsating negative pressure treatment applied in a transparent acrylic cylinder (50×16 cm) on one arm. The cylinder was circulated with water at 42.5°C, leaving an air pocket inside the device. Pulsating pressure between 0 and −40 mm Hg was generated in the air pocket inside the cylinder.

Results. Two groups of 10 patients were studied. Warming was started shortly after induction of general anaesthesia. The two methods performed similarly during the first 60 min, with a mean 0.7° decrease in core temperature. The tympanic temperature curve in NM group then increased and returned to baseline (37°C) by 120 min. The temperature of SM group increased more slowly, reaching 36°C by 120 min ($P<0.05$).

Conclusion. Warm water and pulsating negative pressure was significantly better at treating hypothermia during laparotomy than forced-air warming.

Br J Anaesth 2007

Keywords: equipment, warming devices; hypothermia; surgery, laparotomy; temperature, body

Accepted for publication: November 1, 2006

Mild hypothermia both during and after laparotomy has several adverse effects.[1 2] Various non-invasive methods have been tried to prevent and treat mild perioperative hypothermia. As most metabolic heat is lost through the skin surface, active cutaneous heating is the main principle of most devices. Circulating-water mattresses, forced-air warmers, resistive heating, and radiant warmers are all in clinical use.[2 3] Recently, systems using a combination of heat and mild constant negative pressure to increase the cutaneous blood circulation have been proposed. Recovery from mild hypothermia has been shown to be moderately accelerated by this method.[4–6] The mechanism is claimed to be that mechanical distension of peripheral vessels overrides thermoregulatory vasoconstriction,[7] thus improving the transfer of heat from the external source to the peripheral blood and thence to the core of the body. However, further studies showed no effect of negative pressure in this context.[8] A possible explanation of this is provided by the finding that continuous negative pressure reduces blood flow locally via the veno-arterial reflex, which causes arterial vasoconstriction in response to the distension of venous vessels.[9 10] We hypothesized that pulsating negative pressure would perform better by increasing blood flow and heat transfer. In this clinical study, we

†*Declaration of interest.* According to University Innovation policy, a patent was filed in connection with the development of the apparatus used in this study (UK). Later, patents were filed in several other countries, including Europe and USA. A limited liability company in Norway, Thermonor, is pursuing the commercial interests. E. B. Rein and M. Filtvedt have commercial interests in an eventual product.

have tested the hypothesis that negative pulsating pressure and warm water applied locally could effectively reverse perioperative hypothermia. A well documented, efficient forced air-warming system, that is, Bair Hugger®, was used as a comparator.

Materials and methods

The study was carried out at the main operating theatre at Ullevål University Hospital. The regional ethics committee approved the study, and written informed consent was obtained from all patients. All equipment used in this study met the criteria laid down by the Norwegian Directorate for Civil Protection and Emergency Planning and was also approved by the Department of Electro-Medical Equipment at Ullevål University Hospital.

Subjects

Patients who were to undergo laparotomy for major abdominal surgery were asked to participate in the study. Each operation was expected to last for at least 2 h. All patients were fasted from midnight the day before. Criteria for exclusion were skin lesions on the right arm, vascular diseases, diabetes, fever, arthritis, and rheumatic diseases. The patients were randomized into two groups by a computer program (Microsoft® Office Excel). One group of patients received treatment with locally applied warm water and pulsating negative pressure, called the new method (NM). The other group was treated using the Department's normal method, which was forced-air warming using warm air blankets. This was called the standard method (SM).

Experimental design

Patients treated with NM rested in the supine position on the operating table. The right arm was abducted 70–90° and positioned inside a custom-built tube-shaped transparent Plexiglass chamber, 50×16 cm (Figs 1 and 2). The chamber was sealed to the proximal part of the arm by a neoprene collar, which was attached to an adapter (10×16 cm). An elastic rubber sleeve ran from the proximal neoprene collar to the Plexiglass cylinder making the tube watertight. Warm water at 42.5°C was circulated between the cylinder and a thermostat-regulated water-bath. The water-bath was connected to the chamber by two insulated latex hoses. A peristaltic pump circulated the water at 3.5 litre min^{-1}. Two independent alarm systems were attached to prevent accidental overheating. The chamber was three-quarters full of water, leaving an air pocket from which the air could be evacuated to give negative pressure. The pressure inside the chamber was pulsated between 0 (=ambient pressure) and −40 mm Hg. The chamber was connected to an adjustable medical suction device. A pair of computer-controlled magnetic valves were connected between the chamber and the suction device. A computer program controlled the opening and closing of the valves. When a magnetic valve opened, air was evacuated by the suction and pressure fell inside the tube. After 10 s the valve was closed, another valve opened, and air from the surroundings could freely pass into the tube for the next 7 s as pressure rose back to atmospheric pressure. The pressure inside was measured continuously. The pressure waveform had a saw tooth shape. The cycle of 10 s on and 7 s off was based on empirical data from pilot studies.

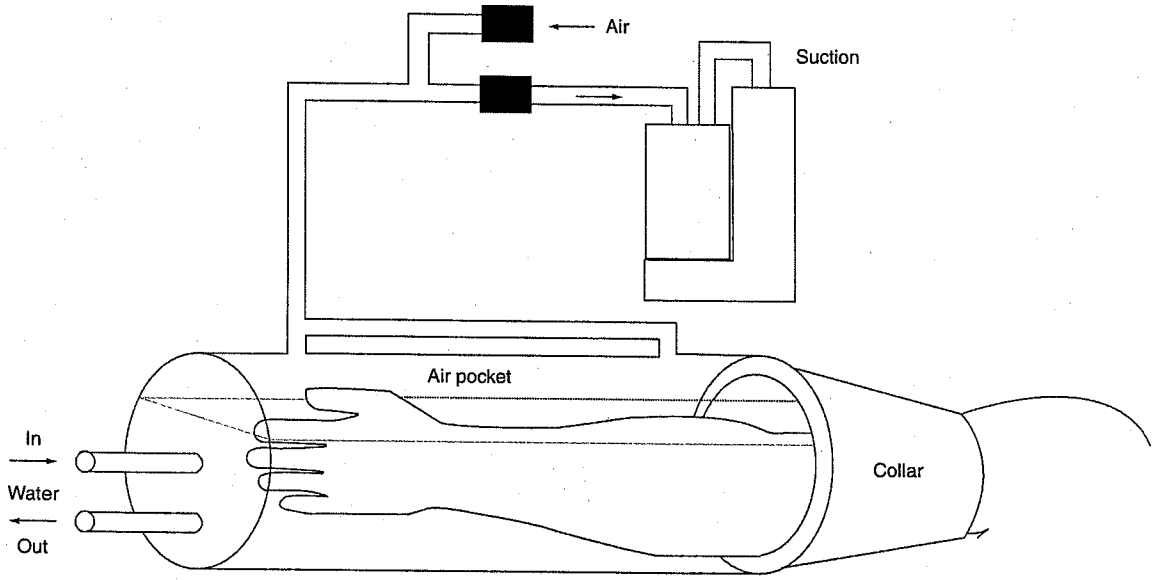

Fig 1 Cylindrical transparent Plexiglass chamber (50×16 cm), sealed to the upper arm by a neoprene collar attached to an adapter (10×16 cm). An elastic rubber sleeve ran from the proximal neoprene collar to the Plexiglass cylinder making the tube watertight.

Fig 2 Picture taken from head-end of operating table showing new method used on patient: Plexiglass cylinder on patient's right arm. Hoses for evacuation of air (top) and circulating water (end) attached to cylinder. The Anaesthesiologist is covering patient's face. (Photograph reproduced with the patient's permission.)

Table 1 Comparison of the two groups, NM and SM, n=10 in each group. Data are median (range) or mean (SD)

Variables	New method	Standard method
Subjects		
Age (yr)	70 (41–81)	63 (43–87)
Weight (kg)	70.20 (11.49)	66.67 (16.19)
Height (cm)	1.75 (0.09)	1.68 (0.08)
BMI (kg m^{-2})	23.0 (18.3–26.4)	21.0 (18.3–36.1)
Operation method		
Laparatomy	10	10
Additional thoracotomy		2
Operation variables		
Core temperature before anaesthesia (°C)	36.7 (36.4–37.0)	36.9 (35.8–37.0)
Total duration of surgery (h)	2.9 (1.4–6.8)	2.7 (1.3–4.83)
Total duration of anesthesia (h)	3.9 (2.2–6.8)	3.7 (2.3–6.0)
Time from anaesthesia to warming (min)	20 (10–45)	30 (20–75)
Room temperature (°C)	22 (21–24)	21.0 (20–22)
Room humidity (%)	39 (31–55)	42 (32–66)
Haemoglobin (g dl^{-1})	13.9 (10.3–15.8)	13.3 (10.3–15.2)
Fluids given i.v. (ml)*	5750 (3500–10 650)	5800 (4300–8300)
Diuresis (ml)	303 (0–1063)	244 (0–1175)
Blood loss (ml)	475 (150–2500)	500 (200–1140)
Peritoneal lavage (litre)	2 (1–2)	2 (0–3)

*Ringer acetate, Makrodex, Haemaccel, Voluven, NaCl, SAG, Haes.

The SM group received the hospital's standard treatment, forced-air warming, using Bair Hugger® warm air blankets. The blankets covered the thorax and abdomen above the incision, both arms, neck, and sometimes the legs if practical. The anaesthetic personnel operated this system and were instructed to prevent hypothermia according to hospital standards and to follow their normal routine. This is to use forced air at 43°C and maximal air flow until normothermia is re-established.

All i.v. fluid was pre-heated to 37°C in a heating chamber before infusion, as was fluid for peritoneal lavage. Blood was warmed during infusion with a blood warmer. Swabs were pre-heated in a liquid water-bath, holding 37°C. This is standard procedure and was identical in both groups. The operating room temperature and humidity was set centrally for entire theatre wing and measured locally and noted regularly during surgery (Table 1). Active warming with SM or NM was started as soon as possible after induction of anaesthesia.

Measurements

The core temperature was measured continuously using a tympanic probe[11] (Exacon, model 8940, Denmark) starting before induction of anaesthesia, and data were fed online to a computer and recorded at 2 Hz. To standardize the measurements as far as possible the probe was inserted by the same person every time. The probe was securely fastened to the ear and neck with adhesive plaster to avoid movement of the probe during patient handling. Cotton was inserted into the distal 1–2 cm of the external ear canal to isolate the probe and prevent air from the surroundings from interfering with the readings. Because measurements were made continuously and displayed real-time on a computer screen, any sudden non-physiological change in temperature, for example, if a probe was pulled away from the tympanic membrane was seen and corrected. In addition, oesophageal and rectal temperature probes were used when possible to confirm the readings of the tympanic probe.

Data analysis and statistics

Because the surgical equipment generated some electrical noise, the continuous data from the tympanic temperature were manually read and edited after the study. The temperature was noted at 10 min intervals for analysis. The primary endpoint was the tympanic temperature at 120 min. The changes in tympanic temperature between baseline (at induction of anaesthesia) and 120 min (ΔT after 120 min) were compared between the two groups. The differences in temperature change between the groups at 60 min after induction of anaesthesia (ΔT after 60 min) were also calculated. The Wilcoxon two-sample test was used to test for significant differences in ΔT between the two groups. Even though the patients were randomized to the two treatment groups, possible differences in patient characteristics and other confounding factors were tested by a *post hoc* stepwise multiple linear regression analysis. All anthropometric variables and all variables from Table 1, in addition to the warming method, were possible explanatory variables in the analyses and ΔT was the dependent variable. All the analyses were performed using the statistical program SPSS. Differences were considered significant at $P<0.05$.

Results

Three patients whom we approached refused to participate in this study. Twenty patients, 9 females and 11 males

agreed to take part. Patient characteristics, type of operation, and operation variables are listed in Table 1. There was a gender difference between the two groups. In the NM group, there were three female patients age [median (range)] 73 (70–81) yr and seven male patients age 73 (70–81) yr. In the SM group, there were six female patients age 57.5 (43–87) yr and four male patients age 77 (63–78) yr. Active warming started on average 10 min later in the SM group, and lasted for 175 (range 130–280) min in the NM group, as compared with 246 (range 130–350) min in the SM group. Warming was shorter in the NM group because the warming device had to be turned off to prevent over-heating of patient. Duration of anaesthesia and surgery was similar in the two groups (Table 1).

The new method resulted in significantly faster re-establishment and maintenance of body temperature than the standard method after 120 min. Stepwise multiple linear regression showed that the only significant variable in addition to the warming method was patient height. ΔT decreased by 2°C for each metre increase in height (P=0.036). When the results were adjusted for this variable, the difference in ΔT between the two methods increased from 0.92°C to 1.00°C.

Figure 3 shows averaged normalized values for both groups. The highest registered starting temperature in each group was 37.0°C, and the two groups were therefore normalized by addition, making all experiments start at 37.0°C. In the NM group, the mean temperature initially decreased by 0.7°C in the course of 50 min, before increasing and returning to the starting value after 130 min. In the SM group, the temperature decreased 1°C beyond 80 min and then remained stable at this level throughout the operation.

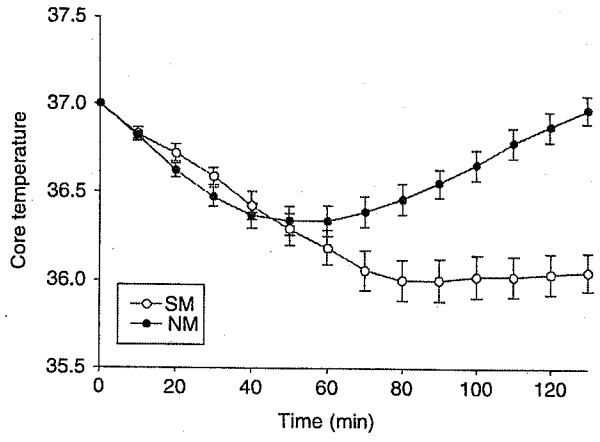

Fig 3 Averaged normalized tympanic temperatures from both groups. The graphs are normalized by adding, making all experiments start at 37.0°C. Induction of anaesthesia is at 0 min. Error bars are plus and minus one standard error.

Discussion

The main finding in this study is that locally applied warm water and pulsating negative pressure is significantly better than the Bair Hugger® forced-air warming system in preventing and treating mild perioperative hypothermia during abdominal surgery. Abdominal surgery is known to cause mild hypothermia, probably because of the prolonged duration of surgery, the large incision required and the frequent use of peritoneal lavage.[12] Most of our patients were operated on as part of cancer treatment. These patients are often elderly, a patient group which is known to be prone to hypothermia.[13] In our study, the median ages were 70 yr in NM group and 63 yr in SM group. We would have expected our patients to suffer from mild hypothermia if no treatment had been given.

Without treatment, intraoperative hypothermia develops in three phases.[1 14] In phase 1, hypothermia results from a core-to-peripheral redistribution of heat after induction of general anaesthesia (GA) and subsequent immediate vasodilatation. General anaesthesia also reduces the threshold for cutaneous heat-loss protective vasoconstriction to a level below current body temperature leading to dilation of arterioles and AV-anastomoses. This produces a decrease in body core temperature of approximately 1.5°C within the first hour if unopposed. In phase 2, the core temperature decreases linearly, but at a slower rate, because body heat loss exceeds heat gain. In phase 3, after 3–5 h of anaesthesia, heat loss equals heat gain. A stable plateau with core temperatures about 2–3°C below baseline is usually reached, depending on the temperature in the environment and how well the patient is protected from heat loss. In our study, both groups showed an initial decrease in core temperature (ΔT). None of the patients were pre-heated, and therefore, the temperature decrease was expected. The temperature decrease in the SM group was 0.3°C larger and a nadir was reached 30 min later at 1.0°C below baseline levels. There may be several different explanations for this. Warming was started 10 min later in the SM group, allowing the temperature to decrease further than in the NM group before warming could take effect. The reason for this delay was washing and draping of the surgical field before the airflow blankets could be applied. Airflow blankets ideally need to cover as close to the surgically washed and draped field of the abdomen as possible in order to utilize a maximum area of skin exposure for best effect. This conflict with sterile draping and delay in application is not present for the NM group during laparotomy when an arm is used for heat application. This practical aspect was also illustrated by coincidence in our study as two of the patients (in the NM group) needed extension of the surgical field into thorax. However, both methods were equally easy to start and operate. In both groups, the average temperature decreased at about 0.8°C h^{-1}, thus a 10 min delay would equal a decrease in temperature of just under 0.2°C.

Another explanation of difference in temperature decrease could be the modest difference in BMI. Preoperatively, a patient with a high BMI tends to be more vasodilated than a patient with a low BMI. This is due to the insulating effects of fat tissue, which makes the dissipation of heat in adipose people dependent on high skin blood flow. This decreases the core-to-peripheral temperature gradient and results in a smaller decrease in temperature during phase 1 of perioperative hypothermia. However, the stepwise multiple linear regression analyses did not identify BMI as a significant variable for the differences in core temperature after 120 min. There was also a gender difference between the two groups, with more females, and a wider age range (43–87 yr), in the NM group. Several studies on human temperature regulation have shown gender differences.[15] These studies are mainly on eumenorrheic women. Not many studies have been performed on gender differences in the older population during perioperative hypothermia. A study on subjects that were awake showed that all thermoregulatory response thresholds, that is, sweating, vasoconstriction, and shivering, were 0.3°C wider in women.[16] A study on thermoregulatory vasoconstriction during nitrous oxide/isoflurane anaesthesia showed a lower threshold for elderly patients, but no gender difference.[17] Our regression analysis did not reveal an effect of age or gender. However, the small sample size means that this analysis had limited power. The last, and most obvious, explanation for the difference in temperature decrease between the two groups is a difference in efficacy between the two warming methods. The NM brought the core temperature in all patients back to baseline levels. In the SM group, the average core temperature reached a plateau at 1.0°C below baseline level. This is still better than expected without any treatment, confirming that forced-air warming does have an effect.

Forced-air warming has been extensively tested,[1 3 14 18–26] and is now the preferred warming system in many hospitals.[3] During laparotomy, a large section of the abdominal skin surface is unavailable for forced-air heating, in addition to the part of the patient that is in contact with the operating table. The efficacy of the forced-air warming system is dependent on a large skin surface for heat transfer. In addition, heat uptake is dependent on skin blood flow in the heated area. Another limiting factor is the thermal conductivity of air, which is low, 0.025 ($W\ m^{-1}\ °C^{-1}$).

There may be several explanations for the efficacy of the NM. The use of water increases heat transfer because the thermal conductivity of water (0.600 $W\ m^{-1}\ °C^{-1}$) is 25 times higher than that of air. Water also connects better with the skin, entering every fold and groove. Finally, and perhaps most important, the pulsating negative pressure probably increases blood flow. A pilot study done in our laboratories, using the ultrasound Doppler method, showed that local blood flow could be increased by at least 43% by pulsating the negative pressure in the same manner as done in our study. The increase in blood flow can be explained by an increase in the pressure difference between the arterial and venous system and by avoidance of the veno-arterial reflex, which constricts the arterioles when the veins are distended.[3 10] An additional feature may be pooling of blood in the veins, bringing more blood closer to the surface for heat exchange.

In conclusion, the new method using warm water and pulsating negative pressure was significantly better in preventing and reversing hypothermia during laparotomy than forced-air warming (Bair Hugger®).

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